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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,682	08/15/2005	Tetsuo Nagano	P26478	5929

7055 7590 04/09/2008

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EXAMINER	
SOLOLA, TAOFIQ A	
ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
04/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/519,682	NAGANO ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *07 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-10 are pending in this application.

Priority

The claim of priority based on JP 2002-198197 filed 7/8/02, is not valid. Therefore, the claim is denied.

Claim Rejections - 35 USC § 112

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims lack adequate support in the specification. R3 and the phraseologies "a substituent for trapping" and "a ring structure for trapping" are not defined in the specification so as to ascertain the structures of the substituent and the ring. While the substituent is not exemplified or otherwise in the specification, the ring (formed by R1 and R2) is defined by examples in page 7. Also, R3 is defined as preferred examples. However, "[e]xemplification is not an explicit definition." The specification must set forth the definition explicitly and clearly, with reasonable clarity, deliberateness and precision, *Teleflex Inc. v. Ficosa North Am Corp.,* 63 USPQ2d 1374, (Fed. Cir. 2002), *Rexnord Corp. v. Laitram Corp.,* 60 USPQ2d 1854 (Fed. Cir. 2001).

The specification fails to disclose 'how' the step of selecting a combination of R1, R2 and R3, is performed. There is no conclusive evidence in the specification that the invention is reduced to practice. By adding the missing information the rejection would be overcome. However, the addition of new matter would raise the issue of new matter rejection.

Claim 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement to make and use the compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claim.

"'In the context of determining whether sufficient "utility as a drug, medicant, and the like in human therapy" has been alleged, It is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the [compounds and the utilities] as obviously correct." *In re Jolles*, 628 F.2d 1327, 1332 (Fed. Cir. 1980), citing *In re Novak*, 306 F.2d 924 (CCPA 1962); see 340 F.2d 974, 977-78 (CCPA 1965).

"A specification disclosure which contains a teaching of the manner and process of making and using the invention . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), Id. at 1566, quoting *Marzocchi*, 439 F.2d 220, 223 (CCPA 1971); *Fiers v. Revel,* 984 F.2d 1164, 1171-72 (Fed. Cir. 1993), quoting *Marzocchi*, 439 F.2d at 223; see also *Armbruster*, 512 F.2d 676, 677 (CCPA 1975); *Knowlton*, 500 F.2d 566, 571 (CCPA 1974); *Bowen*, 492 F.2d 859 (CCPA 1974); *Hawkins*, 486 F.2d 569, 576 (CCPA 1973).

Where there is "no indication that one skilled in the art would accept without question [the instant compounds and method of use] and no evidence has been presented to demonstrate that the claimed products do have those effects *Novak*, 306 F.2d at 928, an applicant has failed to sufficiently demonstrate sufficient utility and therefore cannot establish enablement."' *In re Rasmusson,* 75 USPQ2d 1297 (CAFC 2005). The claimed invention is not enabled without undue experimentation for the following reasons:

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered. *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC, 1988): "The factors to be considered [in making an enablement rejection] have been summarized as a) the breadth of the claims, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and, the quantity of experimentation necessary, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex prate Formal*, 230 USPQ 546. The breath of the claims includes compounds in claims 1-16. The nature of the invention is using the compounds as pharmaceuticals.

The specification fails to disclose 'how' the step of selecting a combination of R1, R2 and R3, is performed. Not all the substituents of the compounds are defined in the specification. Some are defined by functions, others by examples. To make and use the compounds as claimed one of ordinary skill must perform trial and error assays using every element in a textbook of organic chemistry starting from the beginning to the end, changing the combinations of the substituents and determining the oxidation potential of each combination to know if the potential is within the prescribed range. Even then, there is no conclusive evidence such combination(s) would work. This is deemed undue experimentation under the US patent practice.

There is no absolute predictability or established correlation between the claims and the specification disclosures. The uncertainty presents one of ordinary skill in the art with obstacles and prevents her from accepting the invention on its face. Predictability in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. *See Ex parte Mass*, 9 USPQ2d 1746, (1987).

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding any of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. See the Examiner's suggestion above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite. It is not possible to determine the structures of the compounds that are included and/or excluded by R3 and the phraseologies "a substituent for trapping" and "a ring structure for trapping". Therefore, it is not possible to ascertain the metes and bounds of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Minta et al., J. Biol. Chem. (1980), Vol. 264(14), pp. 8171-78.

Minta et al., disclose similar compound and process of making thereof. See FLUO-1, wherein R3 is OH.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagano et al., WO 99/51586 (US equivalent 6,525,088 B1).

Nagano et al., disclose similar compounds, and process of making thereof. See the abstract, col. 19 and claim 1, wherein R3 is carboxylic acid.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagano et al., WO 01/62755 (US equivalent 6,903,226 B2).

Nagano et al., disclose similar compounds, and process of making thereof. See col. 3, lines 34-40, wherein R3 is carboxylic acid or ester.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagano et al., EP 1 069 121 A1.

Nagano et al., disclose similar compounds, and process of making thereof. See the abstract, and page 3, wherein R3 is carboxylic acid.

In above rejections, compounds of the prior arts are presumed to have the following properties absent a showing to the contrary: the combination of

R^1, R^2, and R^3 provides:

(1) substantially high electron density of the benzene ring to which said groups bind so that the compound represented by the formula (I) is substantially no fluorescent before the trapping of proton, a metal ion, or an active oxygen species, and

(2) substantially reduced electron density of the benzene ring to which said groups bind so that a compound after the trapping, which is derived from the compound represented by the formula (I), is substantially highly fluorescent after the trapping of proton, a metal ion, or an active oxygen species).

The compounds have

the oxidation potential of said benzene ring before the trapping of proton, a metal ion, or an active oxygen species is less than 1.40 V, and oxidation potential of said benzene ring after trapping of proton, a metal ion, or an active oxygen species is 1.40 V or higher, and said oxidation potential of said benzene ring increases by 0.20 V or higher after the trapping, under a sufficiently basic condition so that the hydroxy group of the xanthene ring can become a complete anion when R^6 is hydrogen atom.

And

~~or 2~~, wherein the oxidation potential of said benzene ring before the trapping of proton, a metal ion, or an active oxygen species is less than 1.70 V, and the oxidation potential of said benzene ring after the trapping of proton, a metal ion, or an active oxygen species is 1.70 V or higher, and the oxidation potential of said benzene ring increases by 0.20 V or higher after the trapping, under a sufficiently acidic condition so that the hydroxy group of the xanthene ring can exist in a non-dissociation state when R^8 is hydrogen atom.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

/Taofiq A. Solola/

Primary Examiner, Art Unit 1625

March 31, 2008

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